Treatment of Patients with Metastatic Melanoma by Lymphodepleting Conditioning Followed by Infusion of TCR-Gene Engineered Lymphocytes and Subsequent Peptide Immunization

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Scientific Abstract:

The alpha and beta chains of the T-cell receptors (TCR) from highly avid anti-melanoma T-cells were isolated and used to construct retroviral vectors. Anti-gp100 and anti-MART-1 expressing TCR vectors were produced in the PG13 packaging cell line and shown mediate high efficiency gene transfer into primary human lymphocytes. Engineered PBL or TIL were demonstrated to be biologically active by HLA class I restricted recognition and lysis of melanoma tumor cells. Based on these observations the following clinical protocol is proposed.

Patients with metastatic melanoma who are HLA-A2 positive will receive a nonmyeloablative but lymphocyte depleting preparative regimen consisting of cyclophosphamide and fludarabine, and then will be treated by the adoptive transfer of autologous TIL or peripheral blood lymphocytes that have been genetically engineered to be reactive with melanoma tumor antigens gp100 or MART-1. Following adoptive cell transfer, all patients receive high-dose IL-2 and then will receive gp100 and/or MART-1 specific peptide vaccinations. This study will evaluate the potential therapeutic role of this treatment, the survival of the transferred cells, and any potential toxicities associated with the protocol.

The primary objective will be to determine whether patients with metastatic melanoma who are HLA-A2+ and who receive either TIL plus HD IL-2 plus gp100 or MART-1 or PBL plus HD IL-2 plus gp100 or MART are able to produce modest numbers of clinical responses. Additional objectives include; determination of any differences in the effectiveness of the anti-gp100 versus anti-MART-1 vector transduced cells, determination of the survival of TCR gene-engineered cells, and to determine if the treatment is associated with toxicity.